ISSN 0377-4910

ICMR BULLETIN

Vol. 27, No. 3

March, 1997

COMMUNITY HEALTH CELL LIBRARY AND DOCUMENTATION UNIT BANGALORE.

EMERGENCY CONTRACEPTION

A woman would prefer to prevent an unwanted pregnancy rather than having an abortion or carrying the pregnancy to term. No amount of legal or religious restrictions, social stigma or lack of access to professional care can stop her if she decides to seek termination of an unplanned pregnancy. Society and the health care providers should help in preventing abortions. A late abortion is particularly distressing for both the woman and the professionals involved in her care. In spite of this, it is surprising that an estimated 40-60 million women seek termination of pregnancy every year[1]. Unfortunately, a large percentage of the induced abortions, particularly in developing countries, are performed by unqualified persons under unsafe conditions. As a result, the woman faces a risk of death perhaps 100-500 times greater than the woman who has access to a skilled operator working in aseptic conditions. In fact, unsafe abortion is one of the greatest neglected problems of health care in developing countries and a serious concern to women during their reproductive lives. At least 70,000 of the approximately 580,000 maternal deaths that occur annually are a consequence of complications of unsafe abortion procedures.

The available methods of fertility regulation are quite safe and effective, and their use can help couples to decide when and how often to allow pregnancy to occur. In addition to the regular methods of contraception, there are contraceptives available, commonly referred to as emergency contraception, which can be used postcoitally and provide a back-up in individuals at risk of unplanned pregnancy. Indications for emergency contraception include unprotected intercourse, failure of barrier method, missed oral contraceptive pills, and sexual assault. Emergency contraception has therefore rightly been referred to as "the Casualty Department of Family Planning" as it offers a last chance, secondary method of contraception to prevent an unplanned pregnancy[2].

Increased adolescent sexual activity in recent years has resulted in a corresponding increase in pregnancy, childbirth and abortion, as well as increase in the sexually transmitted diseases (STDs). How to deal with and especially how to prevent these problems are major concerns and topics of debate among parents and at all levels of the community. The access to and appropriate use of contraceptives including emergency contraceptives can help prevent unwanted pregnancies and could save the women from the agony and embarrassment of resorting to induced abortions. Most couples are not aware that contraception even after coitus is possible. Surveys conducted by the International Planned Parenthood Federation in 1994 have shown that, in South Asia, only 20 per cent of the family planning associations provide emergency contraceptive services, as compared to 100 per cent in Europe. The Survey also indicated that the women who sought emergency contraceptive services were in the age group of 15-30 years[3].

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24/6/97

Couples in the reproductive age group need to be educated about the available emergency contraceptives and women have to be empowered to make and exercise their own choice of contraceptive methods. They need to be reminded that pregnancy during the adolescent years can severely limit their future as well as of their offspring. Infant mortality is highest among babies born to the young mothers. It is essential therefore to enable women to have more control over their reproduction and to exercise their full rights.

Recent studies have shown that if emergency contraceptives are made known and are also generally available, many women who are subjected to unprotected intercourse, would rather use them than resort to abortion later. For reproductive health care managers, therefore, it is important to ensure the availability of such methods and services.

This review provides information on the available methods of emergency contraception, barriers to their use, and the rising international interest to include emergency contraception as a part of the reproductive health care package and make it more widely available to the potential users so as to prevent unwanted pregnancies and consequently induced abortions.

Available Methods

Emergency contraception includes methods that can be used to prevent pregnancy following an unprotected act of sexual intercourse. The other terms frequently used to express emergency contraception are "postcoital" contraception and "morning-after pills". However, these terms are generally misleading as they do not convey the correct timing of use of the available methods and the important message that emergency contraception should not be used regularly. The term emergency contraception dispels the fear that the user had missed the chance of averting an unwanted pregnancy if she did not wait until the morning-after or by having delayed the treatment beyond the morning-after. The term emergency contraception also emphasizes that such methods are for only emergency use and not intended for regular use.

The two methods of emergency contraception which are currently in use are: steroid hormone pills and copper-releasing intrauterine devices (Cu-IUDs)[4]. Among the steroidal methods, high-dose estrogens, estrogen-progestogen combination (Yuzpe regimen), and progestogen-only pills, are available in many countries and their postcoital use can reduce substantially the incidence of pregnancy. The use of Cu-IUDs offers a more effective method of preventing pregnancy in comparison to the use of hormonal methods. This method may be useful when the woman plans to continue using the device as a long-term method of contraception.

High-Dose Estrogens

High-doses of estrogens were the first hormonal method, pioneered in the mid-1960s by Haspels, for emergency use to prevent pregnancy[5]. The first reported clinical trial was done on a 13-year old rape victim who was given 50 mg of diethylstilbestrol (DES). Subsequently, studies to identify the most effective and safe estrogen and to optimize the dose and duration of treatment followed. Some of the synthetic, natural and conjugated estrogens which have since been used are: DES (25-50 mg/day, 4-5 days), ethinyl estradiol (2-5 mg/day, 3-5 days), and conjugated equine estrogens (30-50 mg/day, 2-5 days). Estradiol benzoate (12.5 mg) combined with 10 mg estradiol phenylpropionate has also been used as an emergency contraceptive agent[6].

The estrogens are generally administered in two dosages for up to five days. Treatment, initiated within 72 hours of the unprotected intercourse, is very effective. The pregnancy rate is generally less than one per cent with most of the regimens.

The use of high doses of estrogens induces severe side effects which are related to the drug load. The incidence of nausea and vomiting is reported by over 50 per cent and 25 per cent, respectively, of women on the first day of treatment. Headache, dizziness, breast tenderness, and irregular bleeding are also reported by some of the women. In cases of treatment failures, about 10 per cent of the resultant pregnancies are likely to be ectopic.

The high incidence of side effects and prolonged duration of treatment have restricted the use of high doses of estrogens as an emergency method of contraception.

Yuzpe Method

In the early 1970s Yuzpe showed that a single dose of 100 mg of estrogen and 1.0 mg of dl-norgestrel rendered the endometrium out of phase[7]. Since then the use of estrogen-progestin combination, also referred to as the Yuzpe method, is the most commonly used method of emergency contraception. The method is simple,

relatively inexpensive and could be made readily available as the steroids involved are available world-wide and contraceptive delivery systems have already been established in many countries.

Different combinations of estrogens and progestins have been tried in various countries, however, the most typical formulation contains 200 mg of ethinyl estradiol and 2.0 mg of dl-norgestrel (or 1 mg of levonorgestrel) which is given in two divided doses. The treatment is initiated within 72 hours of the unprotected sex and the second dose is repeated 12 hours later. When pills containing lower doses of ethinyl estradiol and levonorgestrel (or norgestrel) are available, proportionately increased number of pills are taken. Treatment should not be delayed unnecessarily as efficacy may decline over time. However, the timing of taking the first dose should be such that taking the second dose 12 hours later will not be inconvenient.

The failure rate of the Yuzpe method ranges from 0.2 to 2 per cent if calculated by the conventional method, *ie.* the percentage of pregnancies occurring amongst treated women irrespective of the day of coitus[8]. On the other hand, in the trials that used information on the time of coitus relative to ovulation and have compared the number of pregnancies observed with the number expected, it was shown that the Yuzpe regimen reduced the chances of pregnancy by about 75 per cent[9]. The lower contraceptive efficacy of the Yuzpe regimen in comparison to the regular contraceptive methods is because with the use of emergency contraceptive pills the pregnancy rate is based on a one-time use, it cannot be directly compared to failure rates of regular contraceptives, which represent the risk of failure during a full year of use.

The side effects of the Yuzpe regimen are comparable to those seen after high-dose estrogen, but their incidence is lower. Typical side effects are nausea and vomiting. Less common side effects include breast tenderness, abdominal pain, dizziness and headache. A recent study has shown that in the combination regimen, the incidence of side effects with the use of pills containing levonorgestrel is significantly less as compared to the use of pills containing dl-norgestrel[10]. Although the side effects are uncomfortable for many women, very few women experience serious medical problems. Similarly, the short exposure to steroids does not appear to alter blood clotting mechanisms. The high doses of steroids used in the combination regimen do not increase the rate of spontaneous abortion if treatment fails and they are ineffective after implantation has occurred. No teratogenic effects have been reported after 'occasional' postcoital use of combination regimen. The percentage of ectopic pregnancies among the failures is higher than among a normal pregnant population. It is therefore essential to rule out the possibility of ectopic pregnancy in all cases of failures of emergency contraceptive pill users.

Emergency contraceptive pills should not be given to a woman who has a confirmed pregnancy, primarily because there will be no effect. According to the most recent guidelines from the World Health Organization (WHO), there are no other known medical contraindications to the use of emergency contraceptive pills. The dose of hormones used in the combined estrogen-progestin regimen of emergency contraception is relatively small and the pills are used for a short time, so the usual contraindications associated with use of combined oral contraceptives for regular contraception do not apply. If an estrogen-free preparation is desired, an option is to give 750 mg of levonorgestrel within 72 hours of intercourse, followed by a second dose 12 hours later.

Proprietary preparation of the estrogen-progestogen combination are now licensed for emergency contraception in the United Kingdom, Germany, Norway, Finland, Sweden, Switzerland, New Zealand and Hungary[11]. However, several brands of combined oral contraceptives contain the same hormones as used in the combination regimen but the doses are lower resulting in women using these brands having to take a greater number of pills.

Progestogen-only Pill

Levonorgestrel (0.75 mg) tablets are available in several countries for occasional contraceptive use. Its contraceptive action is probably due to the combined effects on pituitary-ovarian function, endometrium and on cervical secretion[12]. Studies carried out in the early 1970s showed that the frequent postcoital use of levonorgestrel was associated with a high incidence of cycle disturbances. However, subsequent studies showed that when used as an 'occasional' method of postcoital contraception, the menstrual irregularities with levonorgestrel were much less. The initial report evaluating the contraceptive efficacy of levonorgestrel in

emergency contraception provided very encouraging results. Treatment with a single 0.6 mg dose, given within 12 hours after unprotected intercourse, had a pregnancy rate of 3 per cent in 205 treated women[13].

A prospective randomized trial compared the effectiveness and side effects of two tablets of levonorgestrel, each taken 12 hours apart, with those of the Yuzpe regimen among women requesting emergency contraception within 48 hours of unprotected intercourse[14]. A total of 424 subjects were recruited into the Yuzpe group and 410 subjects into the levonorgestrel group. The contraceptive efficacy of levonorgestrel was similar to that of the Yuzpe regimen. The failure rates were 2.6 per cent and 2.4 per cent, respectively. With both treatments, pregnancy rates tended to be slightly lower among women who initiated treatment within 24 hours after intercourse than among those who began between 24 and 48 hours.

The side effects like nausea, vomiting and breast tenderness with this method were similar to but less frequent than those found with the Yuzpe regimen. The trial is being replicated in a multinational study sponsored by the WHO. If the findings are confirmed, levonorgestrel could represent an improvement over currently available methods of emergency contraception[12].

Copper-IUDs

Use of Cu-IUD as a method for emergency contraception was introduced in late 1970s by Lippes and coworkers[15]. The contraceptive effectiveness of IUDs, when used in emergency contraception, is primarily due to their ability to prevent implantation which is attributed to endometrial changes resulting from the presence of the device and the copper ions, and possibly a direct embryotoxic action of copper.

The emergency use of a Cu-IUD is a highly effective method to prevent pregnancy, the failure rate is probably no higher than 0.1 per cent[16]. Additional advantages of this method include its longer time frame for administration, *ie.* it can be inserted up to 5 days after intercourse or up to 48-72 hours later than hormonal methods. The longer time span is because of the ability of an IUD to prevent implantation. It also has the additional advantage of providing contraceptive protection for many years. Postcoital IUD insertion is particularly useful when the hormonal methods are no longer effective.

Some of the disadvantages of the IUD for emergency contraception are: (i) it may be difficult to insert particularly in young and nulliparous women; (ii) some abdominal discomfort may occur; (iii) risk of infection, particularly in cases of multiple sexual partners and of rape; and (iv) in some cases relatively long-term contraceptive protection may not be desired.

The service delivery implications raised by the method, however, may be challenging, particularly in some developing countries. In general, there has been a gradual decrease in the age at first sexual encounter as a result of which many young and nulliparous women require emergency contraception. For such a population, IUD may not be the first choice for emergency contraception.

Potential Future Methods

The requirements of an ideal emergency contraceptive are: high effectiveness, free of side effects and menstrual disturbances, longer sex-treatment interval, easily administrable form, preferably single administration, and affordable. The currently available methods do not meet all the requirements of an ideal emergency contraceptive. However, it should not discourage prospective clients to use the available methods to avert unwanted pregnancy. The side effects of emergency contraceptive methods generally subside within 24 hours and therefore may not carry the same weight as with regular methods of contraceptionas. Moreover emergency contraceptives may be needed only once in a lifetime. Nevertheless, there is an urgent need for new and better methods of emergency contraception. The hormonal methods which are being investigated include an antiprogestin mifepristone and a progestogen danazol.

Antiprogestogens

Progesterone is indispensable for the establishment and maintenance of pregnancy. Its major physiological role is to prepare the uterus for implantation of the fertilized ovum and then to nurture it for its development. Progesterone also has a direct role in the intra-ovarian regulation of folliculogenesis and ovulation as well as transport of fertilized egg through the Fallopian tubes[17]. Thus, any substance interfering with the synthesis, secretion or peripheral actions of progesterone would have antifertility effects.

Mifepristone (RU 486) is a potent progesterone antagonist which blocks the action of progesterone both at the endometrial and pituitary levels. Treatment with mifepristone either in the early or mid-luteal phase of the menstrual cycle invariably disrupts follicular development[18]. The preovulatory rise in serum levels of estradiol and luteinizing hormone is either attenuated or completely blocked and ovulation is arrested. On the other hand, treatment with mifepristone during the early luteal phase, impairs endometrial development and prevents implantation[19]. The properties of mifepristone to arrest ovulation as well as prevent implantation make it an ideal candidate for emergency contraception.

Studies conducted under the aegis of the WHO have confirmed the potential value of mifepristone as an emergency contraceptive. In two clinical trials, one comparing mifepristone with Yuzpe regimen[20] and the other mifepristone with Yuzpe regimen and danazol[21], mifepristone was found to be the most effective. No pregnancy was observed among the 597 women (402 at one centre and 195 at the other) who were exposed to the risk of pregnancy and were given a single dose of 600 mg mifepristone within 72 hours of unprotected intercourse. Analysis of the data from the centre where 195 women were enrolled showed that at least 72 women had had intercourse within three days after ovulation. On the other hand, among 589 women who received the Yuzpe regimen nine pregnancies occurred (pregnancy rate: 1.5%), and among 193 women treated with danazol nine pregnancies occurred (pregnancy rate: 4.7%). In addition, the women who used mifepristone reported less nausea and vomiting and fewer other side effects than did those receiving the Yuzpe regimen. The incidence of nausea and vomiting was slightly less in women treated with danazol in comparison to those treated with mifepristone. In 42 per cent women treated with mifepristone, the menstrual cycle length was prolonged by three or more days, compared to 13 per cent in women treated with Yuzpe regimen. The prolongation of menstrual cycle length could be due to the extension of the follicular phase resulting in delayed ovulation.

To assess the efficacy and side effects of lower doses of mifepristone in emergency contraception, WHO has carried out a multicentre study, involving 11 centres which recruited 1717 women, evaluating three doses, 600 mg, 50 mg and 10 mg[22]. It was estimated that among these women some 10 per cent would have become pregnant without treatment. According to interim results all doses appeared to be equally effective and prevented about 90 per cent of the pregnancies which would have occurred without treatment. These studies need to be extended to determine whether the treatment would still be effective in women presenting with a delay of up to five or six days after unprotected intercourse and also to determine as to how often mifepristone or related antigestagen could be used in one cycle without causing disturbances in the menstrual cycle rhythms. Studies are being also planned to compare low doses of mifepristone with both the Yuzpe regimen and the levonorgestrel treatment to assess advantages and disadvantages of these methods of emergency contraception.

Danazol

Danazol is a progestogen with antigonadotrophic activities. It also prevents implantation by rendering the endometrium out of phase. The use of danazol for emergency contraception has been found to be more effective as compared to the Yuzpe regimen[23]. Among the 990 women who were treated with 800 mg danazol (two doses of 400 mg at 12 hour interval) within 72 hours of the unprotected intercourse, only 17 pregnancies occurred (pregnancy rate: 1.7%). Increase in the dose of danazol further reduced the pregnancy rate. Among the 730 women treated with 1200 mg dose (3 doses of 400 mg each at 12 hour interval) only 6 pregnancies occurred (pregnancy rate: 0.8%). In this study, the pregnancy rate among the 407 women treated with the Yuzpe regimen was 2.2 per cent (9 pregnancies). The incidence of side effects such as nausea, vomiting and breast tenderness was also less in women treated with danazol in comparison to those treated with Yuzpe regimen.

A more recent study, however, failed to confirm these findings[21]. The pregnancy rate in the danazol treated group (600 mg given twice, 12 hours apart) was 4.7 per cent, which was nearly the same as the number expected with no treatment. This study questions the usefulness of danazol in emergency contraception and suggests a need for further research to determine its potential as emergency contraceptive agent. Danazol is contraindicated in women with undiagnosed or abnormal bleeding, impaired liver, kidney or heart function, or porphyria, epilepsy or migraine.

The development of better methods for emergency contraception is therefore a challenging task and requires collaboration between investigators and organizations active in the field.

Potential Users

A woman who would like to avert a pregnancy but gets exposed to unprotected sex is likely to use emergency contraception rather than resorting to abortion later on. All women in the reproductive age would therefore prefer to have access to this secondary method of contraception, even before they may need it. Decrease in the age at the first sexual encounter, and increased demand for abortion by young girls indicate that adolescents are the most vulnerable population in greatest need for contraceptives and contraceptive services.

In India, about 275 million people (approximately 30% of the total population) are between the ages of 10-24 years, of which 90 million are between 15-19 years[24]. Only 19 per cent of the married women between 15-24 years of age use any form of contraception. As a result, 17 per cent of teenagers start childbearing[25]. These young Indian adolescents seem to contribute substantially to the estimated 1-4.4 million abortions induced on adolescent women in developing countries each year. They are the potential users of emergency contraception.

There are no realistic estimates on the use of emergency contraception in India. Nearly all the data related to sexuality, use of emergency contraception and attitude to take chances comes from the more developed countries. In a survey conducted in the United Kingdom, on 167 pregnant women aged 13-19 years, it was observed that only 12 per cent of the pregnancies were planned, 73 per cent were unplanned and in another 15 per cent the teen was equivocal at the time of conception about preventing pregnancy[26]. Many of the teenage couples do not use contraception during their first sexual experience. They do not plan ahead or think about possible consequences, such as unintended pregnancies and STDs. They need to be informed of the available options to prevent pregnancy and provided with reliable contraceptives and contraceptive services.

Another possible reason to provide emergency contraception is the increasing use of condom by young couples, particularly by those with multiple partners. In the United Kingdom, a survey conducted by the Office of Population Censuses and Surveys in 1993 showed that after the Health Education Authority began warning the people about the acquired immunodeficiency syndrome (AIDS) the teenagers switched their main method of contraception from the pill to the condom[27]. Since the failure rates with condom or the barrier methods are, in general, relatively higher, the women will require a secondary method of contraception in the event of breakage or slippage of the barrier method.

Pregnancy complications and maternal and infant mortality are also common among adolescents. Infants born to adolescent mothers are at higher risk of low birth weight, prematurity and stillbirth. Teenage pregnancy is a result of lack of knowledge about family planning, lack of access to contraception, and lack of reproductive health services, as well as sociocultural factors. It is important therefore that besides health education, increased emergency contraceptive services, including emergency contraception, are made available to all women particularly young couples.

Expanding Access to Emergency Contraception

Despite the facts that emergency contraceptives have been available for almost 20 years and are safe and effective to prevent substantial number of unwanted pregnancies, they have remained "the world's best contraceptive secret". Non-availability of registered products for emergency contraception, lack of awareness among women and health care providers that contraception following intercourse is feasible, and service-related factors hamper accessibility and wider use of emergency contraceptives. The misconceptions such as that emergency contraception is an abortion, and its use promotes irresponsibility and a promiscuous life-style particularly among adolescents also contribute to underutilization of emergency contraception to prevent unintended pregnancies. Some of the barriers to the availability and use of emergency contraception and what needs to be done to expand access to emergency contraception are discussed below.

Product Availability

In India, no pharmaceutical company is marketing emergency contraceptive pills or Cu-IUDs specifically packaged or labelled for use for emergency contraception. Though oral contraceptive pills are officially available for regular contraceptive use, their use as emergency contraceptive drugs has not been included in the National Family Welfare Programme. Even in the developed countries, where the contraceptive prevalence rate is relatively high, not many pharmaceutical companies have been marketing emergency contraceptives.

In countries, like India, where preparations of emergency contraceptives are not available, if the available oral contraceptive pill is to be used as an emergency contraceptive, the whole packet has to be opened to provide the desired dose. This would create logistic problems in dispensing and audit. Moreover, some practitioners may not be willing to prescribe the use of oral contraceptives for a non-approved indication, thus hampering wider availability and use of emergency contraception.

It is essential that emergency contraception is included in the family welfare programme and appropriate products and services are made available for that purpose. This should attract the pharmaceutical industry to market preparations for emergency contraception. There should not be any legal restrictions in marketing emergency contraception as the available methods prevent pregnancy rather than producing miscarriage. Moreover, the available emergency contraceptive pills and Cu-IUDs have been found to be effective and safe.

User's Perspectives and Awareness

Awareness that contraception is possible even after coitus is an important requirement for the use of emergency contraception. Lack of awareness as well as precise information about emergency contraception are some of the major barriers to the use of emergency contraception. The potential users of emergency contraception may have heard of emergency contraception but may not be aware that the hormonal methods of emergency contraception is simply a larger dose of the steroids which are used in regular oral contraceptives and their use is safe and effective; emergency contraception is not an abortion and the medication is not taken for termination of pregnancy; and the hormonal methods have to be used within 72 hours and the Cu-IUD within five days of the unprotected intercourse. It is also important for the potential user to know how to obtain emergency contraception in a timely fashion.

In India, a survey of 1125 urban and 575 rural women in the reproductive age group showed that only 8 and 3 per cent of the women in the two groups, respectively, knew about emergency contraception[28]. Even in countries where overall contraceptive prevalence rate is high, knowledge about emergency contraception is rather low. In the United Kingdom, for example, where emergency contraceptives have been available for almost 12 years, 24 per cent of the population surveyed had no knowledge of the existence of the emergency contraception, and only 10 per cent knew that the method had to be used within 72 hours of the unprotected intercourse. Similarly, knowledge that IUD can also be used for emergency contraception was much less as compared to emergency contraceptive pill. In New Zealand, a survey among 200 women seeking pregnancy termination showed that 38 per cent had not heard of the emergency contraception and 41 per cent did not know where to obtain it[29]. Similarly, a survey conducted in Princeton University, showed that many students confused pills dispensed for emergency contraceptive use with the abortifacient mifepristone[30].

Failure to use emergency contraception is not always a matter of ignorance[11]. In a recent study from the United Kingdom amongst 167 pregnant teenagers (aged 13-19 years) requesting pregnancy termination or having their first antenatal visit, 135 girls had heard of emergency contraception but 119 did not obtain it. In just over two-thirds of these 119 teenagers, the girl was aware that she was at risk of pregnancy but 'took a chance' rather than obtain emergency contraception[26]. Clearly, counselling about the risk of unplanned pregnancy following unprotected intercourse must be given greater emphasis in sex education, family planning counselling, *etc.*

The main reason underlying lack of awareness of the available methods and the willingness to use the methods of emergency contraception is, of course, the failure of family planning services and providers and of the educational system to give information about emergency contraceptives to potential users.

A comprehensive survey of the knowledge or awareness of emergency contraception in the general population is very essential. It should then be followed by a well-designed and intensive information, education and communication campaign among the potential users. The available methods should be publicized through meetings, workshops and group discussions, during counselling for family planning, and through media such as radio and television to create awareness about emergency contraception. The pharmaceutical companies should, in addition to manufacturing and marketing the drugs, share responsibility in increasing awareness among the potential users and the providers. In addition, contraceptive clinics for teenagers need to be established which can provide services and counselling for all methods of fer-

tility regulation. The latest scientific findings regarding the advantages and disadvantages of the available contraceptive methods need to be brought to their attention.

However, it may be emphasized that it is the woman who has to take the final decision whether she would like to have easy access to the product and the services. The providers, the pharmaceutical companies and the government are generally ambivalent towards the provision and use of emergency contraception. In the USA, a coalition of women's health advocates and professional associations in health fields organized a successful campaign to encourage governmental regulatory changes that would promote greater access to emergency contraceptive services.

Provider's Perspectives and Awareness

Another obstacle to wider use of emergency contraception is continued ignorance of the available methods among a large population of the health care providers. In India, a random survey of 342 gynaecologists revealed that only 30 per cent had some awareness about the available options[28]. Similarly, a survey conducted in New Zealand showed that 62 per cent of the women who reported for termination of pregnancy indicated that they would have used emergency contraception if their physician had provided them with a postcoital pill to have had on hand for use after unprotected intercourse, and 57 per cent said they would have purchased such a pill if it were available over the counter at pharmacies[29]. A survey determining the knowledge, attitude and prescribing practices concerning emergency contraception amongst rural and urban general practitioners (GPs) from New South Wales, Australia, indicated that a substantial number of practitioners did not have adequate information about emergency contraception[31]. Amongst those who had some knowledge about emergency contraception, 58 per cent of urban GPs and 52 per cent of rural GPs prescribed the Yuzpe regimen, and some prescribed regimens which had not been adequately studied. Moreover, almost 30 per cent of the urban and rural GPs did not include information about emergency contraception in routine contraceptive counselling. In addition, the survey results suggested that some doctors may not provide information or prescribe emergency contraception, probably because of moral or religious objections.

These findings suggest that the general practitioners and other health care providers need to be informed and trained about the emergency contraception, indications for emergency contraception, management of a request for contraception and followup.

In a country like India, where the doctor-patient ratio is very low, the gynaecologists alone may not be adequate in numbers to counsel on emergency contraception. It may be appropriate to involve other health professionals and if need be educate them about the use of the available methods. This may help in extending services for emergency contraception. The non-governmental organizations (NGOs) can provide significant help in promoting emergency contraception. NGOs can also help in training doctors. Prescription requirement also poses an obstacle to some potential users, which need to be overcome ideally by making the emergency contraceptive pills available off the shelf. In some of the developed countries, the barrier of prescription is overcome by providing 24-hour telephone referrals to nearby sources of emergency contraceptives. Similar facilities need to be established in India.

Improved Services

Where to get an emergency contraception is another essential requirement for its timely use. Many women may know or have heard of emergency contraception but may not know how to access it within 72 hours of its need. In many countries emergency contraception can be obtained only on prescription, which is not easy to get within 72 hours of unprotected intercourse particularly over the weekends. Moreover, many young couples may feel embarrassed to talk to the doctors and may therefore prefer to take a chance. Some poor women may even lack access to a family planning provider.

Making these methods widely and easily available could have a significant impact upon reducing the incidence of unintended pregnancies. It is essential therefore to make these methods widely available. Emergency contraception would probably be less effective if prescription was made essential. In some countries such as the United Kingdom, New Zealand and Norway, the possibility of making it available over-the-counter from pharmacists is currently under discussion[11]. Another approach, taken in China, is to give barrier method users emergency contraceptive pills prophylactically for back-up use in case of mishap with the barrier method.

In the USA, a toll-free service has been established which provides callers with information about emergency contraceptive methods available in the USA as well as the

names, telephone numbers, and locations of three providers located nearest to them. The hotline is completely confidential, fully automated, and available 24 hours a day.

In India also, confidential access to emergency contraception should be provided through the most practical delivery systems so that people in need of the method can obtain it without delay. Possible avenues of distribution could be pharmacies, family planning clinics, private practitioners, vending machines, and casulty departments of all hospitals and nursing homes. There is also a need to actively advertise the availability of emergency contraception and that health personnel should inform women about it during visits. Hospitals and general practitioners should provide personalized advice about emergency contraception to the users of barrier methods for contraception. They should also display conspicuous, well-designed, information, and accurate materials for the public in the waiting rooms. Providing women with leaflets about taking the contraceptive pill correctly and emergency contraception appears to improve significantly their extent of such knowledge. The drug industry should also participate in creating awareness among the potential users about the emergency contraception and in bringing to their attention the emergency contraceptive potential of existing products. Increased knowledge about the available methods and their proper use might reduce the number of unplanned pregnancies.

Ethical Considerations

The three major issues which raise ethical considerations are emergency contraception might be viewed as tantamount to abortion; promotes irresponsibility and promiscuous life-styles; and is targeted mainly at unmarried adolescents[32].

Data from a survey conducted by the International Planned Parenthood Federation (IPPF) amongst its affiliate members indicate that several family planning programmes do not provide emergency contraception because of the mistaken belief that its mode of action is an abortifacient one. For the similar reasons, some women with religious or philosophical objections may be hesitant to use emergency contraception. The health care providers and women with such concepts need intensive counselling. They need to be explained that emergency contraceptives act by way of either preventing ovulation, fertilization or implantation. These methods do not terminate an established pregnancy. In fact, emergency contraceptive pills are not effective after the pregnancy is established. Therefore, even in countries where abortion is not legal, it should be quite ethical to provide emergency methods of contraception.

Another concern raised about emergency contraception has been that when easily available this would be used routinely in lieu of a barrier method, or even the men may pressurize a woman into unprotected sex. These concerns are due to the lack of awareness about the contraceptive effectiveness of the available methods of emergency contraception. The available hormonal methods of emergency contraception are not as effective as regular hormonal methods and should therefore not be used as a substitute for regular contraceptives.

The availability of emergency methods of contraception should also not be viewed as promotion of adolescent sexuality and premarital sex[33]. If the emergency contraceptives were not available, one should consider the consequences when a woman using regular contraception had a contraceptive accident either because the method was not used correctly or the method failed such as when a condom breaks, or a diaphragm or IUD becomes dislodged; when woman is forced to have sex against her will; and when men and women fail to plan ahead.

Similarly, access to emergency contraceptives for adolescents is not an attempt to undermine parental authority and community morals. The demographic and health surveys point to increasing numbers of teenage pregnancies and induced abortions. Moreover, infant mortality is known to be very high among babies born to the young mothers. Pregnancy at a young age may severely affect a woman's entire future. Preventing an adolescent pregnancy should be viewed highly ethical.

Some health care providers have shown concern that access to postcoital contraception will encourage women to stop using a regular contraceptive method. Studies, however, show that this is not the case. Only 8 per cent of women seek repeat use of emergency contraception. Use of the method in this situation may actually serve as an entry point for patients to obtain emergency contraception and to start a regular, reliable method.

In all of these circumstances the ethical course of action is to use emergency contraception to prevent an unplanned pregnancy rather than getting a pregnancy terminated. It may be highly unethical to withhold the benefits of a technology that is less dangerous than either

carrying an unwanted pregnancy to term or undergoing an abortion. In addition, it is equally important to provide to adolescents sex education and education about reproductive physiology, contraceptive practices, and STDs including AIDS.

Consortium for Emergency Contraception

A conference on emergency contraception held in Bellagio in April 1995 highlighted the facts that the use of available methods of emergency contraception can help avert an unwanted pregnancy and consequently an induced abortion[34]. The participants also emphasized that this potential of emergency contraceptives has not been exploited to the full advantage of the women and, therefore, recommended that the government and the NGOs should ensure that women everywhere have access to these safe and effective ways to prevent unwanted pregnancy. The participants called upon family planning providers to include emergency contraception in all family planning programmes and on all national essential drug lists, a recommendation which was acted upon by the WHO Expert Committee on the use of Essential Drugs, within a few months of the meeting.

In response to the need for increased access to emergency contraception, seven international agencies, committed to expand the availability of all safe and effective methods of fertility regulation including emergency contraception, formed a Consortium[35]. These organizations are the Concept Foundation, IPPF, the Pacific Institute for Women's Health, Pathfinder International, the Population Council, the Programme for Appropriate Technology in Health; and WHO. The Consortium's goal is to identify, through model introductions and operation research, the specific "best practices" needed to broaden access to hormonal emergency contraceptives while ensuring their safe and appropriate use. The Consortium's proposed five-year programme of work comprises (i) Establishment of partnership with private industry to market a product for use for emergency contraception and to publicize the product and create awareness among the potential users. The Consortium has decided to promote the use of progestogen-only pill (two tablets containing 0.75 mg each of levonorgestrel) as its use may have fewer side effects as compared to the estrogen-progestin combination pills. (ii) Introduction of emergency contraception in the developing countries. Initially the Consortium partners, jointly with the four developing countries (Kenya, Indonesia, Mexico and Sri Lanka), will design, implement and evaluate introduction strategies, which will then be replicated to other developing countries. The introduction strategies will be tailored to suit the reproductive health needs of individual countries.

In addition to the efforts by the Consortium partners, other international agencies have also initiated programmes to bring emergency contraception into the mainstream of reproductive health care. IPPF has issued substantially liberalized guidelines designed to make emergency contraceptive pills more easily accessible through "the most practical delivery systems" and to remove virtually all contraindications for their use[35]. The Advisory Committee of the US Food and Drugs Administration has declared the Yuzpe method safe and effective and urged its wider availability. This action should facilitate approval of a dedicated product in the USA, and may be in other countries. National publicity campaigns have been launched in many countries to educate women and providers about emergency contraception.

The scope for introducing emergency contraception in India is wide. Steps need to be taken to remove the barriers to the introduction and use of emergency contraception. Strategies need to be formulated which can create awareness about the methods and expand availability. An assessment of potential users information and service needs, regulatory requirements, and service delivery capabilities can provide useful information about the need for emergency contraception as well as help guide the development of an introductory plan.

Conclusions

Emergency contraceptives are methods that can be used to prevent pregnancy following unprotected act of sexual intercourse. The two methods which are currently available in many countries are steroid hormone pills and copper-releasing intrauterine devices (Cu-IUDs). Among the steroidal methods estrogen-progestogen combination (Yuzpe regimen) and progestogen-only pills are safe and effective as only about 2 per cent of the women who take these pills within 72 hours of the unprotected intercourse get pregnant. The use of Cu-IUDs offers a more effective method of preventing pregnancy in comparison to the use of hormonal methods, and the device can be inserted up to 120 hours after the unprotected sex. This method is

particularly useful for women seeking long-lasting contraceptive protection. Despite the facts that emergency contraceptives are safe and effective to prevent substantial number of unwanted pregnancies, their use has been restricted due to the non-availability of registered products for emergency contraception, lack of awareness among women and health care providers that contraception following intercourse is feasible, and service-related factors. Family planning and reproductive health care providers should make emergency contraception a part of the reproductive health care package and make it more widely available. In addition, community and religious leaders, policy-makers and programme managers, women's health advocates, and the public at large should be apprised that emergency contraception is not an abortion, and its use is not meant to promote irresponsibility and a promiscuous life-style particularly among adolescents but instead is a method to reduce the chances of unintended pregnancies and consequently induced abortions. It must also be emphasized that emergency contraception should be reserved for emergency situations only and not to be used as a substitute for regular contraception. Better awareness about contraceptives including emergency contraceptives and their appropriate usage should help prevent the need for abortion. Further research also needs to be done to develop more effective methods, as well as on innovative service delivery approaches.

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This article has been contributed by Dr. Chander P. Puri, Deputy Director, Institute for Research in Reproduction, Mumbai.

ABSTRACTS

Some Research Projects Completed Recently

Response of sarcoma-180 to *Plumbago rosea (chitraka)*, radiation and hyperthermia

Tumour growth inhibiting and radiosensitizing effects of the alcoholic root extract of *Plumbago rosea*, gamma radiation and hyperthermia were studied in experimental tumours in mice. Response to treatment was assessed on the basis of tumour regression, volume doubling time, growth delay and tumour free survival. Sarcoma-180 tumours were produced in Balb/c mice by intradermal injection of $5x10^5$ viable sarcoma-180 cells. Ehrlich ascites carcinomas were propagated by intraperitoneal injection of tumour cells into young adult Swiss albino mice.

The alcoholic root extract of *P. rosea* was effective in inhibiting exponentially growing sarcoma-180 solid tumours. A dose of 75 mg/kg intraperitoneally for 10 days was found to be safe and effective in increasing tumour cure and growth delay. *Plumbago* extract (75 mg/kg) had an additive effect with hyperthermia (43^0 C for 30 min) but a subadditive effect with gamma radiation (10 Gy) in effecting tumour cure and long-term survival of mice bearing sarcoma-180. Tumour cure and volume doubling time and growth delay of partially responding tumours significantly increased after combined treatment of the extract, radiation and hyperthermia above that produced by bimodality treatments.

Even where the extract individually was not very effective as an antitumour agent, it acted as a good radiosensitizer increasing the radiosensitivity of Ehrlich ascites carcinomas. It produced a synergistic effect in increasing the tumour inhibition and animal survival from 10 to 50 per cent. The active component plumbagin, a napthoquinone derivative from *P. rosea* was effective in inhibiting the growth of Ehrlich ascites carcinoma in mice and this effect could be enhanced by combining the drug with radiation. A total dose of 9 mg/kg, given in 3 fractions of 3 mg/kg each, was found to be optimum for plumbagin when used alone or as an adjuvant to radiotherapy. Plumbagin in combination with radiation (7.5 Gy) significantly increased the induction of micronuclei in Ehrlich ascites tumour cells *in vivo* as compared to that induced by single modality treatments. The bimodality treatment produced synergistic increase in micronuclei count at all time points studied (24 to 72h).

Plumbagin treatment resulted in an immediate increase in the S-phase population of cells. Combination of plumbagin with radiation induced reproductive death of proliferating cells and G_2-M block. The increase in micronuclei from 24 to 72 h after combination treatment probably reflected the delayed expression of the cytogenetic damage when the affected cells enter division after G_2-M block. This could contribute to the higher tumour response and tumour free survival after combination treatment as compared to individual modality treatments.

The study thus indicated that *P. rosea* could be a promising drug for human cancer therapy, it has a remarkable radiosensitising effect and requires detailed investigation.

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Publication

Uma Devi, P., Soloman F.E. and Sharada A.C. *In vivo* tumour inhibitory and radiosensitizing effects of an Indian medicinal plant, *Plumbago rosea* on experimental mouse tumours. *Indian J Exp Biol 32*: 523, 1994.

Flow cytometry in archival tumour material

DNA contents and cell cycle distribution were measured in 27 routinely processed paraffin embedded biopsy specimens of prostatic adenocarcinoma and 18 of breast carcinoma using DNA flow cytometry. The analysis of proliferative activity, which is defined as flow cytometric S and G_2-M fractions was also carried out to determine whether these have any independent prognostic value or not.

Twelve of the 27 (44.4%) prostatic carcinoma and 6 of the 18 (33.3%) breast carcinoma specimens yielded $>10^5$ cell/mm^3 which were processed further for analysis of S phase fraction (SPF) and G_2-M phase fraction.

SPF was found to be between 19 and 36 per cent in prostatic carcinoma specimens (the mean being 28.9%). Near diploid tumours had significantly higher SPF compared to hyper- and hypo-diploid tumours. Hypo-diploid tumours had higher G_2-M fractions compared to near diploid and hyper-diploid tumours. Near diploid tumours had a higher mean S+G_2-M fractions compared to hypo- and hyper-diploid tumours. There was a significant difference between the mean values obtained for SPF when grade III and IV prostatic tumours were compared. All the 6 breast carcinomas were grade III tumours and near diploid breast carcinoma tumours had a significantly higher mean S+G_2-M fraction compared to hypo-diploid tumours.

The ploidy status, SPF and S+G_2-M were found to be associated with reevaluated histological grade of tumours. The ploidy, proliferating fractions and histological grade had individual prognostic significance. It is concluded that there was a direct correlation between the incidence of aneuploidy (hyperploidy) in prostatic adenocarcinomas and Gleasons's grade. The high proliferative activity was an independent predictor of high histological grading in prostatic carcinomas. There was no correlation between the ploidy status and histological grade of breast carcinoma.

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ICMR NEWS

The following meetings of various technical committees/groups of the Council were held :

Meetings of the Scientific Advisory Group (SAG)/ Task Forces (TFs) held at New Delhi :

SAG of the Division of Non-Communicable Diseases	February 26, 1997
TF on Epidemiological Study of Child and Adolescent Psychological / Psychiatric Disorders in Rural and Urban Areas	March 13-14, 1997
TF on Collaborative Study on Prevalence of RTI / STD (Hospital based)	March 13-14, 1997

Meetings of the Project Review Group (PRG)/Expert Committee :

PRG of District Nutrition Project for Prevention and Control of Micronutrients Deficiency Disorders	February 22-23, 1997 (at Allahabad)

Expert Committee on Pan Masala	February 24, 1997 (at New Delhi)

Participation of ICMR Scientists in Scientific Events:

Dr. V.P. Sharma, Director, Malaria Research Centre, Delhi, participated in the XXXVII Executive Committee Meeting of the Scientific Committee on Problems of the Environment (SCOPE) at London (February 19-21, 1997).

Dr. Kalyan Banerjee, Director, National Institute of Virology, Pune, participated in the International Conference on Emerging Infectious Diseases in the Pacific Rim at Bangkok (March 6-8, 1997).

Dr. B.N. Saxena, Additional Director-General, ICMR, participated in the International Symposium on Post-coital and Post-ovulatory Contraception at Budapest (March 6-7, 1997). He also participated in a Symposium on Safe Motherhood in India at Stockholm (March 8-9, 1997).

Appointments :

Dr. P.K. Das took over as Director of the Vector Control Research Centre, Pondicherry w.e.f. February 13, 1997.

Dr. H.N. Saiyed took over as Director of the National Institute of Occupational Health, Ahmedabad w.e.f. February 13, 1997.

ICMR AIDED SYMPOSIA/SEMINARS/WORKSHOPS/COURSES/CONFERENCES

Symposium/Seminar/Workshop/ Course/Conference	Date & Place	Contact Address
Symposium on Current Trends in Research on Drugs of Herbal and Marine Origin	March 2, 1997; (at Gandhinagar)	Prof. N.S. Parmar, Principal and Professor of Pharmacology, K.B. Institute of Pharmaceutical Education and Research, Gandhinagar-382023.
International Seminar on Frontiers in Surgical Pathology	March 3-5, 1997; (at Chennai)	Dr. Malathy Madhavan, Professor and Head, Department of Pathology, Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences, Chennai-600113.
International Seminar on Psycho-social Issues in Health Care with Special Emphasis on Psycho-social Oncology	March 6-8, 1997; (at Thiruvanantapuram)	Dr. P.T. Latha, Organising Secretary of the Seminar, Regional Cancer Centre, Thiruvanantapuram-695011.

COUNCIL'S TRAINING PROGRAMMES FOR 1997-98

Leprosy

At the Central JALMA Institute for Leprosy, Agra:

- Training Course on National Leprosy Eradication Programme for Medical Officers (February 24-March 7 and September 15-26, 1997).

Virology

At the National Institute of Virology, Pune:

- Diploma in Medical Virology (July 1997-May 1998).

Reproductive Biology

At the Institute for Research in Reproduction, Mumbai:

- Training Course on Research Methods in Clinical Trials of Newer Contraceptives (April 14-25, 1997).
- Workshop on Genotoxicity (August 28-29, 1997).
- Workshop on Basic Molecular Biology for Clinicians (December 2-11, 1997).

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Certificate Course on Endocrinological Techniques and their Applications (August 1-September 15, 1997).

Nutrition

At the National Institute of Nutrition, Hyderabad:

- M.Sc. in Applied Nutrition (June 1, 1997-February 28, 1998).
- Postgraduate Certificate Course in Nutrition (December 1, 1997-February 28, 1998).

Laboratory Animal Technology

At the National Centre for Laboratory Animal Science, National Institute of Nutrition, Hyderabad:

- Training Course for Laboratory Animal Technicians (June 16-July 31, 1997).
- Training Course for Laboratory Animal Supervisors (September 1-November 29, 1997).

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 27-October 24, 1997).
- Training Course in Blood Group Serology and Blood Bank Methodology for Blood Bank Technicians (August 27-September 26, 1997).
- Training Course in Advanced Haematology and Immunohaematology (October 6-24, 1997).

Occupational Health

At the National Institute of Occupational Health, Ahmedabad:

- Orientation Course on Occupational Health for Industrial Medical Officers (September 30-October 11, 1997).
- Training Course on Environmental Hygiene Practice (November 10-14, 1997).

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Printed and Published by Shri J.N. Mathur for the Indian Council of Medical Research, New Delhi
at the ICMR Offset Press, New Delhi-110029

R.N. 21813/71